Docket No. 043956-0159 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent 5,135,759
Patentee: L.A. Johnson
Issue Date: August 4, 1992

PETITION UNDER 37 C.F.R. §§ 1.182 and 1.183 FOR EXTENSION OF TIME TO FILE AN APPLICATION FOR SECOND INTERIM PATENT TERM EXTENSION

Mail Stop Petitions
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Pursuant to 37 C.F.R. §§1.182 & 1.183, the Patent Owner, United States Department of Agriculture ("USDA"), hereby petitions the United States Patent and Trademark Office ("USPTO") for an extension of time to file an application for a second interim patent term extension ("IPTE"). Under 35 U.S.C. §156(d)(5)(C), Patent Owner's application was due on July 6, 2010. Patent Owner now petitions the Director to grant for USPTO consideration the Patent Owner's application for a second IPTE, which is being filed concurrently with this petition.

STATEMENT OF FACTS

1. U.S. Patent 5,135,759 ('759 patent), is assigned to the USDA and was issued on August 4, 1992. (Exhibit A to attached Affidavit in Support)

2. The original expiration date of the '759 patent was August 4, 2009.

3. USDA has exclusively licensed the '759 patent, in a particular field of use, to the Genetics & IVF Institute ("GIVF").

4. On April 24, 2000, GIVF filed an Investigational Device Exemption ("IDE") with the Food and Drug Administration ("FDA") for use of GIVF's sperm sorting apparatus and process for sorting human sperm on the basis of gender, which are encompassed by the claims of the '759 patent and thereafter commenced its clinical study for the purpose of obtaining regulatory approval from the FDA for its apparatus and process.

5. FDA review of GIVF's sperm sorting apparatus and process was still ongoing in February 2009, six months prior to the original expiration of the '759 patent.

6. Under 35 U.S.C. §156(d)(5), the Patent Owner is entitled to extend its patent beyond the expiration of the patent term as long as it is awaiting regulatory approval from the FDA and satisfies other statutory criteria. 35 U.S.C. § 156(d)(5).

7. In 2009, GIVF engaged patent counsel at the law firm of McDermott Will & Emery LLP ("McDermott") to prepare an IPTE under §156(d)(5)(C) ("IPTE") on behalf of the USDA. Affidavit at ¶2.

8. The USDA filed the IPTE with the USPTO on June 8, 2009, and the USPTO granted the extension on July 28, 2009, extending the term of the '759 patent for one year from the original patent term expiration date, *i.e.*, until August 4, 2010. Affidavit at ¶4.

9. Section 156(d) also entitles the Patent Owner to four subsequent interim extensions, so long as its patented product remains under regulatory review before the FDA. 35 U.S.C. §156(d)(5)(C).

10. Under §156(d)(5)(C), "[e]ach subsequent application shall be made during the period beginning 60 days before, and ending 30 days before, the expiration of the preceding interim extension." 35 U.S.C. §156(d)(5)(C).

11. Under this provision, the period for filing the second IPTE for the '759 patent began on June 4, 2010 and ended on July 6, 2010 (July 4 and 5 were a Sunday and federal holiday, respectively).

12. McDermott uses the Patent Management System provided by Computer Packages, Inc. ("CPI Docketing System") to track information necessary for patent filing and prosecution int post patent-issuance stage. McDermott also relies on the CPI Docketing System, in good faith, to provide notices of filings with the USPTO. Affidavit at ¶5.

13. In this case, information concerning the '759 patent was entered into the CPI Docketing System in a timely manner. Affidavit at ¶6.

14. Nonetheless, the CPI Docketing System did not generate a reminder that the second IPTE for the '759 patent was due on July 6, 2010. Consequently, on July 6, 2010, McDermott did not file the second IPTE for the '759 patent on behalf of GIVF and the USDA. Affidavit at ¶7.

15. On or about July 19, 2010, patent counsel at McDermott discovered that the period for filing a second IPTE under §156(d)(5)(C) had passed. Affidavit at ¶8.

16. On or around July 22, 2010, counsel at McDermott learned that the CPI Docketing System is not programmed to—and cannot automatically track—IPTEs under §156.

Accordingly, the program cannot generate reminders concerning due dates for filing subsequent IPTEs. Affidavit at ¶9.

17. Since discovering that the second IPTE was not filed by July 6, 2010, counsel at McDermott has acted expeditiously to contact the USPTO in order to obtain an extension to file the second IPTE and to prepare this petition and its accompanying application. Affidavit at ¶10.

REMARKS

The issue in this case is whether the USDA may file a request for a second IPTE under 35 U.S.C. §156(d)(5)(C), outside of the filing window set forth in the statute. In considering this question, the USPTO should take into account a few undisputed facts. First, with the exception of timeliness, USDA's application for a second IPTE satisfies all of the statutory criteria for the grant of an extension under 35 U.S.C.§156. Indeed, the USPTO found all of the relevant factors present in 2009. 74 Fed.Reg. 38585. Second, the USDA—through its licensee, GIVF—has diligently sought regulatory approval for its patented product from the FDA. This is not a case, therefore, where the USDA or its licensee somehow sat on its rights before the FDA. Finally, the USDA still has the right to exclude under the '759 patent until, at least, August 4, 2010. This is not a case, therefore, where a Patent Owner seeks to revive a patent that has already expired.

With these facts in mind, the question before the USPTO is very simple: should the USDA be denied the second IPTE, to which it is otherwise entitled, merely because it filed its request one-week—as opposed to one month—before its patent is set to expire. For the reasons set forth below, the USPTO has the discretion to extend the filing period under §156(d)(5)(C) and deem timely the USDA's application for a second IPTE filed on this day.

I. The Language, Structure, and Purpose of §156 Give the USPTO the Discretion to Authorize a Second IPTE Outside of the Statutory Window.

Section 156 itself provides the USPTO with the discretion to authorize the filing at issue in this case. The statute provides in relevant part:

> The owner of record of a patent, or its agent, for which an interim extension has been granted under subparagraph (B) may apply for not more than 4 subsequent interim extensions under this paragraph, except that, in the case of a patent subject to subsection (g)(6)(C), the owner of record of the patent, or its agent, may apply for only 1 subsequent interim extension under this paragraph. Each such subsequent application *shall be made* during the period beginning 60 days before, and ending 30 days before, the expiration of the preceding interim extension.

35 U.S.C. §156(d)(5)(C) (emphasis added). As a general rule, the word "shall" indicates a mandatory, nondiscretionary duty. *Ute Indian Tribe v. Hodel*, 673 F.Supp. 619, 621 (D.D.C. 1987). But statutory interpretation is "not guided by a single sentence or member of a sentence, but look[s] to the provisions of the whole law, its object and policy." *Dole v. United Steelworkers of America*, 494 U.S. 26, 35 (1990). In deciding whether "shall" is mandatory or not, the USPTO should look to the language and purpose of the statute, *Blacklight Power, Inc. v. Rogan*, 295 F.3d 1269 (Fed. Cir. 2002), whether the provision at issue is essential to the statute's purpose, 1A *Sutherland Statutory Construction* §25.4 (7th ed. 2010), and the policy implications of one interpretation versus another. *Holbrook v. United States*, 284 F.2d 747, 752 (9th Cir. 1960). In this case, these factors all point to the same conclusion.

First, the language and purpose of the statute suggest that the USPTO has the discretion to grant the application now at issue. In this very statute, in fact, the USPTO does not treat the word "shall" as inflexible. Section 156 states that "[t]he term of a patent . . . *shall* be extended" as long as certain criteria are met. 35 U.S.C. §156(a) (emphasis added). But the regulations

promulgated pursuant to this statute do not use the word "shall." Instead, they list the same statutory criteria, and state that the "[t]he term of a patent *may* be extended." 37 C.F.R. § 1.720(a) (emphasis added). "There is a strong presumption that when Congress repeats the same word in the same statute, it intends for that word to be given the same meaning." *The Medicines Company v. Kappos*, __ F.Supp.2d __, 2010 WL 1005261, at *5 (E.D.Va. March 16, 2010). If the word "shall" in §156(a) means "may" as the USPTO seems to indicate in its own regulations, then that word should have the same meaning in §156(d)(5)(C) as well. *But see Merck & Co., Inc. v. Hi-Tech Pharmacal Co., Inc.*, 482 F.3d 1317, 1322-23 (Fed. Cir. 2007) (holding that "shall be extended" in §156(a) denotes an imperative, but noting that other parts of §156 "require a more flexible interpretation").

To be sure, there are good reasons to read the word "shall' in this way. As the USPTO has previously explained, §156 is a remedial statute, "intended to restore a part of the effective patent life that has been diminished through delays which are necessary in regulatory review and approval of the product." In re Patent No. 4,146,029 (Comm'r Pat. July 12, 1988) ("*Synchromed*"), at 3. A remedial statute should be "liberally construed . . . to carry out its purpose" so that "justice may be done to both the patentees and the public." *Synchromed*, at 3. Consistent with this remedial purpose, therefore, it is best to interpret §156(d) to permit Patent Owners who otherwise meet the statutory criteria to extend their patents during the FDA review process, rather than interpret the statute to cut off those rights. *See, e.g., The Medicines Company*, __ F.Supp.2d __, 2010 WL 1005261, at *5 (reading the timeliness provisions of Section 156 to extend patent rights, rather than exclude them).

Nearly all of the other time limitations within the Patent Act are treated with precisely this kind of flexibility by the USPTO. The USPTO has read provision after provision as

providing it with flexibility when deciding whether to enforce statutory deadlines. 35 U.S.C. §§ 41(b)(7) & (c)(1) (relating to fees for reviving applications/patents); *id.* §§111(a)(4), (b)(3)(c), & (b)(5) (relating to timing of an application); *id.* §§119(b)(1), (b)(2), (e)(1) & 120 (relating to a claim of priority to an earlier filed application); *id.* §122(b)(2)(B)(iii) (relating to the improper filing of a request for non-publication of a patent application, which may result in abandonment of the application); *id.* §133 (relating to the timing of response to USPTO actions during patent prosecution; *id.* §151 (relating to timing of payment of issue fee after the application has been allowed); *id.* §§184 and 185 (relating to filing of a patent application abroad for an invention made in the US); *id.* §364(b) (relating to timing of prosecuting foreign applications); *id.* § 371(d) (relating to the timing of filing the fee and/or required documents relating to national stage patent application). Although the language in each of these sections differs from that in §156(d)(5)(C), the point is always the same: when it comes to procedural matters, the Patent Act gives the USPTO flexibility to make decisions that further the purpose of the Act. The same is true of §156(d)(5)(C).

Second, the USPTO has the discretion to permit the USDA's second IPTE because the time window set forth in §156(d)(5)(C) is not essential to §156. In deciding whether a statutory provision is mandatory, many courts ask whether the "requirement is so essential a part of the plan that the legislative intent would be frustrated by noncompliance[.]" *Vaughan v. Winston*, 83 F.2d 870, 872 (10th Cir. 1936). In those instances where the "requirement is a detail of procedure which does not go to the substance of the thing done," it is merely "directory" and not "mandatory." *Id.* In this case, §156(d)(5)(C)'s time-window is nothing more than "a detail of procedure," having nothing to do with the substance of the right at issue—the extension of the patent during a period of regulatory review. In this case, the USDA satisfies all of the criteria for

an extension, it has filed its application during a time when its patent is still in effect, and it does not seek to revive an already expired patent. Under such circumstances, the time window under §156(d)(5)(C) is simply a matter of procedure, not substance.

Finally, reading §156(d)(5)(C) in a way to bar the USDA's request will do far more damage than reading this statute to allow the second IPTE. If §156(d)(5)(C)'s filing window is read to bar the USDA's application, then the '759 patent will expire, even though the USDA has been unable to use its product during the life of the patent simply because it had to await FDA approval. By letting this patent expire, the USPTO will undermine the congressional intent to not prejudice patent owners while the regulatory process works. In contrast, granting the patent extension will impose no harm on the public at all. At present, the public is on notice of the existence of the '759 patent and, thus, is not harmed by an extension of that patent in accordance with the statute. Under such circumstances, the "shall" language in §156(d)(5)(C) should not prevent the USPTO from granting USDA's second IPTE request. *Holbrook*, 284 F.2d at 752 (reading statutory language as "directory," rather than "mandatory" due to the harm to the public of a mandatory reading).

Several cases have reached a similar conclusion about the use of the word "shall." In *Blacklight Power, Inc. v. Rogan*, 295 F.3d 1269 (Fed. Cir. 2002), for instance, the Federal Circuit held that the phrase "[u]pon payment of this sum, the patent shall issue" did not require the USPTO to issue a patent once the payment at issue was made. *Id.* at 1272-73. By looking at the statute as a whole, the court concluded that the PTO had the discretion to withdraw an application in those cases where it appeared that a patent should not issue as a matter of law, even if the applicant had already paid the sum required by the statute. *Id.*

In *Ute Indian Tribe v. Hodel*, 673 F.2d 619, 620 (D.D.C. 1987), the United States District Court for the District of Columbia reached a similar conclusion about a statute using the word "shall". At issue in that case was a judgment fund for Indian Tribes established by Congress. The law provided that the fund "*shall be available* for advance to [the Tribe], . . . as may be designated by the Tribal Business Committee[.]" *Ute Indian Tribe v. Hodel*, 673 F.2d 619, 620 (D.D.C. 1987) (emphasis added). After the Secretary of the Interior denied a request from the Tribal Business Committee for distribution of the funds, the Tribe sued, claiming that the use of the phrase "shall be available" deprived the Secretary of any say over the matter. *Id.* at 621. The district court rejected the Tribe's argument, holding that, in light of the statutory purpose to further the trust relationship between the Tribe and the government, "shall" vested the Secretary with discretion to decide when and how to distribute the funds. *Id.* at 621-22. "Despite the use of the word 'shall,'" the court explained, "the overall background of the statute indicates a non-mandatory interpretation of 'shall' is proper." *Id.* at 622 n.7.

While there are no cases interpreting the "shall" language in §156(d)(5)(C), one recent case out of the Eastern District of Virginia sheds light on the flexibility that Congress intended the USPTO to have in circumstances like the present case. *See The Medicines Company*, __ F.Supp.2d __, 2010 WL 1005261, at *5-8. At issue in *The Medicines Company* was the 60-day filing window under Section 156(d)(1) after a Patent Owner receives permission to commercially use a product. *Id.* at *2. In light of the "remedial nature of the statute at issue," *The Medicines Company* court held that the USPTO abused its discretion when it denied an extension application filed more than 60 calendar days after receipt of FDA approval. *Id.* at *5-8. As the Court explained, "the timing provisions of § 156(d) should be 'liberally construed" to carry out the purpose of the statute. *Id.* at *5. Although the provision at issue in *The Medicines Company*

was different than the one here, the principle is the same. In this case, the only construction that is consistent with the language of §156, that furthers its purpose, and that is in line with public policy is one that recognizes that the USPTO has the flexibility to grant the USDA's request for a second IPTE.

II. This Is An Appropriate Case To Permit the Filing of an Otherwise Untimely Second IPTE.

Having determined that the USPTO has the discretion to grant USDA's request, the only question that remains is whether it should. The answer is clearly yes. Under 37 C.F.R §1.183, the USPTO has the discretion to permit a late filing, when not barred by statute, "[i]n an extraordinary case, when justice requires[.]" But, even if that provision does not apply, the USPTO is still empowered by regulation to address "[a]ll situations not specifically provided for in the regulations . . . in accordance with the merits of each situation[.]" 37 C.F.R §1.1.82.

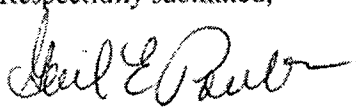
Under either standard, this is a case that requires the USPTO to grant the USDA the relief it seeks. Neither the USDA nor its licensee, GIVF, intentionally sought to miss the deadline under §156(d)(5)(C). Neither knowingly or willfully sought to relinquish its right to extend its patent. Instead, the failure to file within the time window set forth by §156(d)(5)(C) was due to a simple mistake: the IP docketing system relied on to provide deadline notifications was not designed to provide a notice for IPTE applications, and counsel for GIVF missed the deadline. It was a mistake that neither the USDA nor GIVF created or sought to create. There is no prejudice to the public at large from granting this extension, and granting this request actually furthers the purpose of this statute. Under such circumstances, the USDA has shown good cause and extraordinary circumstances warranting the grant of its petition.

In the event that the Office believes a sanction is appropriate as a consequence of the relief requested, patent owner respectfully suggests that an appropriate sanction would be to

reduce the period of the second interim extension by the number of days that this filing is late, *i.e.*, by 21 days (counting from July 6 to July 27). In that way the second interim extension would not extend for the maximum period of one year after the first interim extension as permitted by statute, *i.e.*, to August 4, 2011, but only to July 14, 2011.

The Commissioner is hereby authorized to charge the undersigned's deposit Account No. 502134 for the amount of $400 in accordance with 37 C.F.R. §§ 1.182 and 1.17(f) and any other additional fees associated with this communication or credit any overpayment to Deposit Account No. 502134. A duplicate copy of this sheet is enclosed.

Respectfully submitted,



Gail E. Poulos
Registration No. 36,327
USDA-ARS-OTT
5601 Sunnyside Avenue
Beltsville, Maryland 20705-5131

Phone: 301-504 -5302
Facsimile: 301-504-5060
Date: July 27, 2010

Docket No. 043956-0159 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent 5,135,759
Patentee: L.A. Johnson
Issue Date: August 4, 1992

AFFIDAVIT IN SUPPORT OF PETITION UNDER 37 C.F.R. §§ 1.182 and 1.183 FOR EXTENSION OF TIME TO FILE AN APPLICATION FOR SECOND INTERIM PATENT TERM EXTENSION

Mail Stop Petitions
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Judith Toffenetti, do hereby declare and say as follows:

I am an attorney at the law firm of McDermott Will & Emery LLP and resident in the Washington, D.C. office of that firm. I have personal knowledge of the matters discussed below.

1. A true and correct copy of U.S. Patent No. 5,135,759 (the `759 patent) is attached as Exhibit A.

2. In 2009, GIVF engaged McDermott Will & Emery LLP ("McDermott") to prepare an IPTE for the `759 Patent under §156(d)(5) ("IPTE") on behalf of the USDA, owner of the `759 patent.

3. Along with my colleague Paul Devinsky of McDermott, I prepared the IPTE, which was forwarded to Gail Poulos at USDA for approval and filing.

4. On information and belief, the USDA filed the IPTE with the USPTO on June 8, 2009, and the USPTO granted the interim extension on July 28, 2009, extending the term of the '759 patent for one year from the original patent term expiration date, *i.e.*, until August 4, 2010. A copy of the extension order is attached as Exhibit B.

5. McDermott uses the Patent Management System provided by Computer Packages, Inc. ("CPI Docketing System") to track information necessary for patent filing and prosecution into the post patent-issuance stage. McDermott also relies on the CPI Docketing System, in good faith, to provide notices of filings with the USPTO.

6. On information and belief, information concerning the filing and grant of the IPTE in the '759 patent, including the date to which the term of the patent had been extended, was entered into the CPI Docketing System in a timely manner.

7. Despite the timely entry of docketing information, the CPI Docketing System did not generate a reminder that a second IPTE for the '759 patent was due in a thirty (30) day window set to expire on July 6, 2010. Consequently, McDermott did not timely file a second IPTE for the '759 patent on behalf of GIVF and the USDA.

8. On or about July 19, 2010, I determined that the period for filing a second IPTE under §156(d)(5)(C) had passed. I immediately began to investigate why I had received no docket reminders.

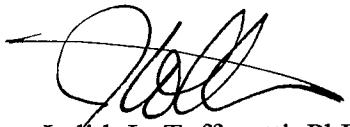
9. On or about July 22, 2010, I first learned that the CPI Docketing System is not programmed to—and cannot automatically track—IPTEs under §156. Accordingly, the program cannot generate reminders concerning due dates for filing subsequent IPTEs.

10. Since discovering that the second IPTE was not timely filed, counsel at McDermott has acted expeditiously to contact the USPTO in order to obtain an extension to file the second IPTE and to prepare this petition and its accompanying application.

All statements made herein are of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Respectfully submitted,

McDERMOTT WILL & EMERY LLP



Judith L. Toffenetti, PhD
Registration No. 39,048

600 13th Street, N.W.
Washington, DC 20005-3096
Phone: 202.756.8000
Facsimile: 202.756.8087
Date: July 27, 2010

US005135759A

United States Patent [19]

Johnson

[11] Patent Number: 5,135,759

[45] Date of Patent: Aug. 4, 1992

[54] METHOD TO PRESELECT THE SEX OF OFFSPRING

[75] Inventor: Lawrence A. Johnson, Silver Spring, Md.

[73] Assignee: The United States of America as represented by the Secretary of Agriculture, Washington, D.C.

[21] Appl. No.: 692,958

[22] Filed: Apr. 26, 1991

Related U.S. Application Data

[63] Continuation of Ser. No. 349,669, May 10, 1989, abandoned.

[51] Int. Cl.[5] A61K 35/52

[52] U.S. Cl. 424/561; 436/63; 436/172; 435/2

[58] Field of Search 436/63, 172; 424/561

[56] References Cited

U.S. PATENT DOCUMENTS

4,083,957	4/1978	Lang	424/105
4,191,749	3/1980	Bryant	424/105

FOREIGN PATENT DOCUMENTS

2145112 3/1985 United Kingdom .

OTHER PUBLICATIONS

Culling, Handbook of Histopathological & Histochemical Techniques, Butterworth & Co., London, 1974, p. 192.

L. A. Johnson, "Flow Sorting of Intact X and Y Chromosome-Bearing Mammalian Spermatozoa," Cytometry, Suppl. 2, p. 66 Abstract (1988).

J. C. Conover and R. B. L. Gwatkin, "Pre-Loading of Mouse Oocytes with DNA-Specific Fluorochrome (Hoechst 33342) Permits Rapid Detection of Sperm-Oocyte Fusion," J. Reprod. Fert. 82: 681-690 (1988).

L. A. Johnson and R. N. Ciarke, "Flow Sorting of X and Y Chromosome-Bearing Mammalian Sperm: Activation and Pronuclear Development of Sorted Bull, Boar, and Ram Sperm Microinjected into Hamster Oocytes," Gamete Res. 21: (1988).

L. A. Johnson et al., "Flow Cytometry of X and Y Chromosome-Bearing Sperm for DNA Using an Improved Preparation Method and Staining with Hoechst 33342," Gamete Res. 17: 203-212 (1987).

R. E. Hinkley et al., "Rapid Visual Detection of Sperm-Egg Fusion Using the DNA-Specific Fluorochrome Hoechst 33342," Dev. Biol. 118: 148-154 (1986).

L. A. Johnson and D. Pinkel, "Modification of a Laser-Based Flow Cytometer for High-Resolution DNA Analysis of Mammalian Spermatozoa," Cytometry 7: 268-273 (1986).

L. A. Johnson, "Gender Preselection in Farm Animals," Research for Tomorrow, 1986 Yearbook of Agriculture, pp. 73-77 (1986).

W. M. Grogan et al., "DNA Analysis and Sorting of Viable Mouse Testis Cells," J. Histochem. Cytochem. 29: 738-746 (1981).

M. R. Loken, "Separation of Viable T and B Lymphocytes Using a Cytochemical Stain, Hoechst 33342," J. Histochem. Cytochem. 28: 36-39 (1980).

Primary Examiner—Douglas W. Robinson
Assistant Examiner—Jean C. Witz
Attorney, Agent, or Firm—M. Howard Silverstein; John D. Fado; Curtis P. Ribando

[57] ABSTRACT

Intact X and Y chromosome-bearing sperm populations of rabbits and swine were separated according to DNA content using a flow cytometer/cell sorter. Sperm viability was maintained by special staining techniques and by sorting and collecting the sperm in nutrient media. The sorted sperm were surgically inseminated into the uteri of rabbits or swine. Of the offspring born from does inseminated with the sorted population of X-bearing sperm, 94% were females. Of offspring born from does inseminated with sorted Y-bearing sperm from the same ejaculate, 81% were males.

26 Claims, No Drawings

EXHIBIT A

METHOD TO PRESELECT THE SEX OF OFFSPRING

This application is a continuation of application Ser. No. 07/349,669, filed May 10, 1989, now abandoned.

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to a method of preselecting the sex of offspring by sorting sperm into X and Y chromosome-bearing sperm based on differences in DNA content.

2. Description of the Prior Art

Gender of animal offspring is important to livestock producers. Because the dairy farmer has little use for most bull calves, the use of sexed semen to produce only females would make milk production more efficient. Swine farmers would produce pork more efficiently if they were able to market only female swine, because females grow faster than males.

In beef cattle and sheep breeds, the male grows at a faster rate than the female and hence is preferred for meat production.

In addition, the ability to specify male or female offspring should shorten the time required for genetic improvements, since desirable traits are often associated with one or the other parent. Planning the sex of cattle offspring is already practiced on a limited basis. This procedure consists of removing embryos from the cow, identifying their potential gender, and re-implanting only those of the desired gender. However, an ability to separate sperm into male-producing and female-producing groups before they are used for artificial insemination could enhance the overall value of offspring produced by embryo transfer.

Every living being has a set of paired chromosomes, which carry all the genetic material necessary to maintain life and also to propagate new life.

All but one pair of chromosomes are called autosomes and carry genes for all the characteristics of the body, such as skin, hair and eye color, mature size, and body characteristics. The remaining pair are called sex chromosomes. They carry the genetic material that specifies gender. One sex chromosome is called X, the other Y.

A sperm from the male or an egg from the female contains one of each pair of autosomes; in addition, in mammals the egg always contains an X chromosome, while the sperm always carries either an X or Y chromosome.

When a sperm and egg unite and the sperm carries the Y chromosome, the offspring is male (XY); however, if the sperm carries an X chromosome when it unites with the egg, the resulting offspring is female (XX).

The only established and measurable difference between X and Y sperm that is known and has been proved to be scientifically valid is their difference in deoxyribonucleic acid (DNA) content. The X chromosome is larger and contains slightly more DNA than does the Y chromosome. The difference in total DNA between X-bearing sperm and Y-bearing sperm is 3.4% in boar, 3.8% in bull, and 4.2% in ram sperm.

The amount of DNA in a sperm cell, as in most normal body cells, is stable. Therefore, the DNA content of individual sperm can be monitored and used to differentiate X- and Y-bearing sperm.

Since the difference in DNA mass in the sex chromosomes of most mammals is the only scientifically validated, measurable difference between X- and Y-bearing sperm, the chromosomal constitution [Moruzzi, J. Reprod. Fertil. 57: 319 (1979)] and/or measurement of DNA mass [Pinkel et al. (1), Science 218: 904 (1982); Pinkel et al. (2), Cytometry 3: 1 (1982); Johnson and Pinkel, Cytometry 7: 268 (1986); Johnson et al. (1), Gam. Res. 16: 1 (1987); Johnson et al. (2), Gam. Res. 17: 203 (1987)] are the only verifiable means other than fertility for determining the sex-producing capability of a population of sperm. The literature describes many physical, biochemical, and functional methods that have purportedly sexed sperm [Amann and Seidel, "Prospects for Sexing Mammalian Sperm," Colorado Assoc. Univ. Press, Boulder (1982)]; several of these methods have been tested for relative DNA content [Pinkel et al., J. Anim. Sci. 60: 1303 (1985); Johnson (1), Theriogenoloy 29: 265 (1988)]. However, no method has been proven in controlled experiments to actually affect the sex ratio of offspring.

Previous studies have demonstrated that the difference in DNA content between X and Y chromosome-bearing sperm can be repeatedly measured and the sperm sex ratio of a sample of semen predicted [Johnson and Pinkel, supra; Johnson et al. (1), supra; Johnson et al. (2), supra; Johnson (1), supra; Johnson (2), Cytometry, Suppl. 2: 66 (Abstract) (1988)]. Verifiable separation by sorting of X and Y sperm based on DNA content has been accomplished with the vole [Pinkel et al. (1), supra; Johnson, In "Beltsville Symposia in Agricultural Research X," P. C. Augustine, H. D. Danforth, & M. R. Bakst (eds.), Martinus Nijhoff, Boston, pp. 121–134 (1986)] and the chinchilla [(Johnson et al. (1), supra]. However, preparation procedures damaged DNA viability. The sorting of sperm nuclei from several mammalian (bull, boar, ram, vole, chincilla) species into separate X and Y chromosome-bearing populations at purities ranging from 92 to 99% has been accomplished [Johnson and Clarke, Gam. Res. 21: 335 (1988)]. Nuclear decondensation and pronuclear development was demonstrated in hamster eggs that had been microinjected with sorted X- or Y-bearing bull, boar, or ram sperm [Johnson and Clarke, supra].

SUMMARY OF THE INVENTION

It is an object of this invention to provide a method for sorting mammalian sperm into X and Y chromosome fractions based on DNA content.

It is a further object of this invention to teach a method of staining the DNA of mammalian sperm while maintaining viability of the sperm.

It is a further object of this invention to provide a sheath fluid adapted to be used in a cell-sorting apparatus while maintaining viability of sperm cells.

It is a further object of this invention to provide a collecting fluid capable of maintaining the viability of sorted sperm cells.

Other objects and advantages of this invention will become readily apparent from the ensuing description.

DETAILED DESCRIPTION OF THE INVENTION

I have now demonstrated the separation, by flow sorting, of intact, viable X and Y chromosome-bearing rabbit and swine sperm populations based on relative DNA content; surgical insemination of the sorted sperm into does; and the subsequent birth of sexed offspring

with a phenotypic sex ratio consistent with predictions based on the relative DNA content of the sorted sperm populations.

A flow cytometer measures the amount of fluorescent light given off when the sperm, previously treated with a fluorescent dye, pass through a laser beam. The dye binds to the DNA. The fluorescent light is collected by an optical lens assembly; the signal is transported to a photomultiple tube, amplied, and analyzed by computer. Because the X chromosome contains more DNA than the Y chromosome, the female sperm (X) takes up more dye and gives off more fluorescent light than the male sperm (Y).

For small differences in DNA to be detected between X and Y, the sperm must pass single file through the laser beam, which measures the DNA content of individual sperm.

In orthogonal flow cytometry, a suspension of single cells stained with a fluorochrome is made to flow in a narrow stream intersecting an excitation source (laser beam). As single cells pass through the beam, optical detectors collect the emitted light, convert the light to electrical signals, and the electrical signals are analyzed by a multichannel analyzer. The data are displayed as multi- or single-parameter histograms, using number of cells and fluorescence per cell as the coordinates.

In order to use an orthogonal flow cytrometric system to differentiate between X- and Y-bearing sperm DNA, a beveled sample injection tip and a second fluorescence detector in the forward position is required [Johnson and Pinkel, supra]. This paper is herein incorporated by reference. The modified system allows one to control the orientation of the flat ovoid sperm head as it passes the laser beam. Elimination of the unoriented sperm by electronic gating enhances precision. Typically, 80% of sperm nuclei (without tails) are properly oriented as they pass the laser beam.

In the modified Epics V flow cytometer/cell sorter, hydrodynamic forces exerted on the flat, ovoid mammalian sperm nuclei orient the nuclei in the plane of the sample stream as they exit the beveled injection tip. Fluorescent signals are collected simultaneously by 90 and 0 degree optical detectors, from the edge and flat side of the sperm nucleus, respectively. For sorting, the sample stream is broken into uniform droplets by an ultrasonic transducer. Droplets containing single sperm of the appropriate fluorescence intensity are given a charge and electrostatically deflected into collection vessels. The collected sperm nuclei then can be used for microinjection into eggs. Since the sperm nuclei have no tails, they cannot be used for normal insemination.

Accurate measurement of mammalian sperm DNA content using flow cytometry and cell sorting is difficult because the sperm nucleus is highly condensed and flat in shape, which makes stoichiometric staining difficult and causes stained nuclei to have a high index of refraction. These factors contribute to emission of fluorescence preferentially from the edge or thin plane of the sperm nucleus. In most flow cytometers and sorters, the direction of sample flow is orthogonal to the direction of propagation of the laser beam and the optical axes of the fluorescence detection. Consequently, fluorescence measurement is most accurate when the sperm fluorescence is excited and measured on an axis perpendicular to the plane of the sperm head [Pinkel et al. (2), supra]. At relatively low sample flow rates, hydrodynamics are used to orient tailless sperm so that DNA content can be measured precisly on 60 to 80% of the sperm passing in front of the laser beam. The modified Epics V system used in this study can measure the DNA content of tailless sperm from most species at the rate of 50 to 150 sperm per second [Johnson and Pinkel, supra].

Intact sperm (with tails), whether viable or nonviable, cannot be oriented as effectively as tailless sperm nuclei [Johnson (2), supra]. However, a 90-degree detector can be used to select the population of properly oriented intact sperm to be measured by the 0 degree detector. Since no hydrodynamic orientation is attempted, the sample flow rate can be much higher, which compensates somewhat for the fact that only 15 to 20% of intact sperm pass through the laser beam with proper orientation. In this invention, the overall flow rate was approximately 2500 intact sperm per second. The intact X- and Y-bearing sperm fractions were sorted simultaneously from the population of input sperm at a rate of 80–90 sperm of each type per second.

It is, of course, of critical importance to maintain high viability of the intact sperm during the sorting process and during storage after sorting but prior to insemination.

Of the factors involved in maintaining sperm viability, the method of staining, the sheath fluid, and the collecting fluid have been found to be especially important.

A nontoxic DNA stain must be selected. A preferred stain is Hoechst bisbenzimide H 33342 fluorochrome (Calbiochem-Behring Co., La Jolla, Calif.). To our knowledge, this fluorochrome is the only DNA binding dye that is nontoxic to sperm. Concentration of the fluorochrome must be minimal to avoid toxicity, and yet be sufficient to stain sperm uniformly and to detect the small differences in the DNA of X and Y sperm with minimal variation. A suitable concentration was found to be 5 μg/ml, but this may be varied from 4 to 5 μg/ml.

The sperm must be incubated with stain at sufficient temperature and time for staining to take place, but under mild enough conditions to preserve viability. Incubation for 1 hr at 35° C. was found to be acceptable, but ranges of 30° to 39° C. would also be effective. Incubation time has to be adjusted according to temperature; that is, 1.5 hr for 30° C.; 1 hr for 39° C.

Sheath fluid used in sorting cells must be electrically conductive and isotonic. A concentration of 10 mM phosphate buffered saline provided the necessary electrical properties, and 0.1% bovine serum albumin was added to enhance sperm viability by providing protein support for metabolism and viscosity for the sperm. The sheath fluid must be free of sugars and excess salts.

Dilution of sperm as occurs in sorting tends to reduce viability of the cells. To overcome this problem, sperm were collected in test egg yolk extender [Graham et al., J. Dairy Sci. 55: 372 (1972)] modified by adjusting the pH and adding a surfactant. Details of the composition of the extender are shown in Example 1. The surfactant is believed to enhance capacitation of the sperm prior to fertilization.

To confirm the DNA content and predict the sex of the offspring of surgically inseminated X or Y sorted sperm fractions, an aliquot of the sorted sperm was sonicated to remove the tails, stained, and the nuclei was reanalyzed for DNA content to predict the proportion of X and Y sperm.

Although the detailed description which follows uses the sorting of rabbit sperm as an example of this invention, it is expected that the sperm of most mammals could be effectively sorted by following these proce-

dures. Those skilled in the art will recognize that minor modifications may be made in the procedure without departing from the spirit and scope of the invention.

Rabbit semen was collected, diluted, and stained with a fluorochrome dye. Sperm were sorted in a modified Epics V flow cytometer/cell sorter.

After being sorted, sperm were surgically inseminated into the uteri of rabbits.

The results obtained by surgical insemination of does with sorted intact sperm are presented in Table I. Recovery of ova 40 hr post-insemination indicated that stained sorted sperm, as well as unstained unsorted sperm, were capable of fertilizing rabbit ova in vivo.

Inseminations were also made to determine the comparability of predicted sex of offspring to phenotypic sex. As the data in Table II indicate, the predictability of the phenotypic sex based on DNA analysis of the separated intact sperm was very high. Reanalysis of the sorted Y population used for insemination indicated that 81% of the sperm were Y-bearing. The sex ratio of offspring from these inseminations was identical to that predicted. These values were significantly different from theoretical 50:50 sex rates ($P<0.003$). Reanalysis of the sorted X-bearing sperm population used for insemination indicated that 86% were X-bearing and 14% were Y-bearing sperm. The phenotypic sex of the offspring from these inseminations was 94% female, which was different from the theoretical 50:50 ($P<0.0003$).

Inseminations were made with sorted X and Y populations that were recombined (recombined X and Y group) immediately before insemination. The assumption was made that the proportions of X and Y in the recombined samples were equal (50:50). The phenotypic sex resulting from the inseminations was 57% female and 43% male (Table II) and was not significantly different from the theoretical (50:50) sex ratio ($P=0.40$).

TABLE I

Fertilizing Capacity of Flow-Sorted Rabbit Spermatozoa After Intrauterine Insemination of Does

Treatment of Sperm	Number of Does Inseminated	Number of Ovulation Points	Number of Eggs Recovered	Number of Eggs Fertilized
Unsorted	2	16	9	9
Sorted	6*	59	46	39

*One doe accounted for 7 recovered and 7 unfertilized eggs.

TABLE II

Predicted and Actual Sex Ratios of Offspring After Intrauterine Insemination of Sorted X and Y Chromosome-Bearing Rabbit Sperm

Treatment of Sperm	Number of Does Inseminated	Number of Does Kindling	Total No. of Young Born	Percentage and Numbers of Offspring: Predicted % Males	Predicted % Females	Actual % Males (N)	Actual % Females (N)
Sorted Y	16	5	21	81	19	81 (17)	19 (4)
Sorted X	14	3	16	14	86	6 (1)	94 (15)
Recombined X and Y	17	5	14	50	50	43 (6)	57 (8)
Total	47	13	51	—	—	47 (24)	53 (27)

The phenotypic sex ratio of offspring born of does inseminated with either sorted X-bearing or sorted Y-bearing sperm was different ($P<0.0002$ for X and $P<0.001$ for Y) from the theoretical (50:50) sex ratio expected from untreated semen.

Embryonic mortality was significant in the does inseminated with sorted intact sperm. With a reasonably high fertilization rate (Table I), one would expect a kindling rate of near 80% and litter size of about six from does of this age and breed. However, the kindling rate across the three treatment groups averaged 28%, with an average litter size of 3.9. The cause of the apparent high rate of embryonic death is though to be due to the fluorochrome binding to the DNA and/or to the effect of the laser beam exciting the DNA bound fluorochrome. Earlier work has shown that sorted vole sperm nuclei that were microinjected into hamster eggs exhibited chromosome breakage in the developing sperm pronucleus [Libbus et al., Mut. Res. 182: 265 (1987)]. Those sperm had been sonicated, stained, sorted, and microinjected, a somewhat more rigorous treatment than the staining and sorting used in this study.

I have demonstrated that DNA can be used as a differentiating marker between X- and Y-bearing sperm, that DNA can be used to accurately predict the sex of offspring from separated X- and Y-bearing sperm populations, and that flow sorting is an effective means for separating viable X- and Y-bearing sperm populations suitable for production of offspring.

The following examples are intended only to further illustrate the invention and are not intended to limit the scope of the invention, which is defined by the claims.

EXAMPLE 1

Semen was collected from mixed breed mature bucks by use of an artificial vagina. Sperm concentration was determined with a hemocytometer. The semen was diluted with Tris buffer, pH 6.9, to a concentration of 10×10^6 per ml. Bisbenzimide H 33342 fluorochrome was added at a concentration of 5 μg/ml. The samples were incubated for 1 hr at 35° C. Intact sperm were sorted on a modified EPICS V flow cytometer/cell sorter. The stained intact sperm were excited in the ultraviolet (UV; 361 and 364 nm) lines of a 5-watt 90-5 Innova Argon-ion laser operating at 200 mW. Data were collected as 256-channel histograms. Sheath fluid was 10 mM phosphate-buffered saline (PBS) containing 0.1% bovine serum albumin (BSA). Sperm were sorted into a test egg yolk extender.

The composition of the extender was N-tris(hydroxymethyl)-methyl-2-amino ethane sulfonic acid, 2.16 g; tris hydroxymethyl aminomethane, 0.51 g; dextrose, 0.1 g; streptomycin sulfate, 0.13 g; penicillin G, 0.08 g; egg yolk, 12.5 ml; Equex STM (Nova Chemical Sales, Scituato, Mass.), 0.5%; and distilled water, 50 ml. This mixture was centrifuged, and only the supernatant was used. The sorted sperm were concentrated by incubating at room temperature for 1 hr, after which the more dilute fraction was removed and the remainder was used for insemination 1 to 4 hr later.

EXAMPLE 2

Mature New Zealand White does were injected with 150 international units of human chorionic gonadotropin (HCG) to induce ovulation, which was expected to occur 10 hr later. Seven hours after treatment with HCG, the does were surgically prepared by injection with Ketamine hydrochloride containing acepromazine and anesthetized under halothane and oxygen. The uterus was exposed by midline incision, and 100 μl of sorted or unsorted sperm was placed into the lumen of the anterior tip of each uterine horn through a 21-gauge needle. Standard management practices were used in caring for the rabbits. These does were sacrificed 40 hr post-insemination; uteri were flushed and recovered eggs evaluated. All fertilized eggs recovered were classified as morula. The results of these experiments are shown in Table I.

EXAMPLE 3

Table II shows the results of inseminations made into the tip of the uterine horn: the number of does that kindled and the phenotypic sex of the offspring compared to the predicted sex. Predicted sex of offspring was based on reanalysis of sorted intact sperm to determine relative DNA content. For reanalysis, the sorted sperm was sonicated for 10 sec and centrifuged at 15,000 g, the supernatant was discarded, and the pellet was resuspended in 9 μM bisbenzimide H 33342. Phenotypic sex of the offspring was determined soon after birth and confirmed at later ages up to 10 weeks. Recombined X and Y is the sorted X and Y sperm populations recombined immediately before insemination.

EXAMPLE 4

Using the methods of Examples 1, 2, and 3, viable swine sperm was sorted into viable X and Y chromosome-bearing populations. Two litters (18 pigs) from surgically inseminated boar semen produced 88% females from X-sorted sperm and 67% males from Y-sorted sperm.

It is understood that the foregoing detailed description is given mainly by way of illustration and that modification and variation may be made therein without departure from the spirit and scope of the invention.

I claim:

1. A method for sorting intact, viable, mammalian sperm into X- and Y-chromosome-bearing populations based on DNA content, the method comprising:
   a) staining intact, viable sperm collected from a male mammal with a fluorescent dye capable of selectively staining DNA in living cells by incubating the sperm with the dye at a temperature in the range of about 30°-39° C. for a period of time sufficiently long for staining to take place uniformly but sufficiently short to preserve viability of the sperm;
   b) passing the sperm into an electrically conductive and isotonic viability-supporting sheath fluid to form a suspension of sperm which are caused to flow singly in a stream of sheath fluid;
   c) passing the sheath fluid containing the sperm before an excitation light source causing the stained DNA to fluoresce;
   d) passing the sheath fluid containing the sperm through both a means for detecting the fluorescence of the stained DNA and also a cell sorting means, the means for detecting fluorescence having at least two detectors arranged such that a first detector determines the orientation of sperm on the basis of magnitude of fluorescence and controls a second detector to measure the DNA content of sperm on the basis of magnitude of fluorescence of those sperm that have been determined to be in a preselected orientation;
   e) selecting by said cell sorting means the sperm having a DNA content corresponding to a desired chromosome which will produce a desired gender of offspring, and separating the selected sperm from nonselected sperm; and
   f) collecting the selected sperm in a viability-supporting collecting fluid.

2. The method of claim 1, wherein said mammal is a rabbit.

3. The method of claim 1, wherein said mammal is a swine.

4. The method of claim 1, wherein said mammal is a bovine.

5. The method of claim 1, wherein said dye is bisbenzimide H33342 fluorochrome.

6. The method of claim 1, wherein said incubation is at a temperature of about 39° C. for a period of about 1 hr.

7. The method of claim 1, wherein said incubation is at a temperature of about 35° C. for a period of about 1 hr.

8. The method of claim 1, wherein said incubation is at a temperature of about 30° C. for about 1.5 hr.

9. The method of claim 1, wherein said sheath fluid is phosphate-buffered saline solution, the solution also containing 0.1% bovine serum albumin to enhance sperm viability.

10. The method of claim 1, wherein said collecting fluid is modified test egg yolk extender.

11. The method of claim 1, wherein said sperm are hydrodynamically oriented in the flow of sheath fluid prior to being passed before said light source.

12. The method of claim 1, wherein said sperm are hydrodynamically oriented in the flow of sheath fluid by passing the fluid in a narrow stream through and out of a bevelled injection tip prior to being passed before said light source.

13. A method to preselect the sex of mammalian offspring comprising:
   a) sorting sperm according to the method of claim 1; and
   b) inseminating a female mammal of the same species as the male mammal with the selected sperm in the collecting fluid.

14. A method to preselect the sex of mammalian offspring comprising:
   a) sorting sperm according to the method of claim 1; and
   b) fertilizing an egg obtained from a female mammal of the same species as the male mammal with the selected sperm in the collecting fluid.

15. The method of claim 1, further comprising eliminating sperm which are not properly oriented with an electronic gating system before sorting by said cell sorting means.

16. The method of claim 1, wherein the flow of sperm through the cell sorting means is regulated by an ultrasonic transducer.

17. The method of claim 1, wherein said sperm are sorted on the basis of X- or Y-chromosome DNA content with about 90% efficiency.

18. The method of claim 1, wherein said sperm are hydrodynamically oriented in the flow of sheath fluid and sperm which are not properly oriented are eliminated by an electronic gating system prior to being passed before said light source.

19. A method to preselect the sex of mammalian offspring comprising:

a) staining intact, viable sperm collected from a male mammal with a fluorescent dye capable of selectively staining DNA in living cells by incubating sperm with the dye at a temperature in the range of about 30°-39° C. for a period of time sufficiently long for staining to take place uniformly but sufficiently short to preserve viability of the sperm;

b) passing the sperm into an electrically conductive and isotonic viability-supporting sheath fluid to form a suspension of sperm which are caused to flow singly in a stream of sheath fluid;

c) passing the sheath fluid containing the sperm before an excitation light source causing the stained DNA to fluoresce;

d) passing the sheath fluid containing the sperm through both a means for detecting the fluorescence of the stained DNA and also a cell sorting means to measure the DNA content of the sperm on the basis of magnitude of fluorescence of the sperm;

e) selecting by said cell sorting means the sperm having a DNA content corresponding to a desired chromosome which will produce the desired gender of offspring, and separating the selected sperm from nonselected sperm; and

f) collecting the selected sperm in a viability-supporting collecting fluid.

20. A method for preparing intact, viable, mammalian sperm for sorting into X- and Y-chromosome-bearing populations based on DNA content, the method comprising staining intact, viable sperm collected from a male mammal with a fluorescent dye capable of selectively staining DNA in living cells by incubating the sperm with the dye at a temperature in the range of about 30°-39° C. for a period of time sufficiently long for staining to take place uniformly but sufficiently short to preserve viability of the sperm.

21. The method of claim 20, wherein said mammal is a swine.

22. The method of claim 20, wherein said mammal is a bovine.

23. The method of claim 20, wherein said dye is bisbenzimide H33342 fluorochrome.

24. The method of claim 20, wherein said incubation is at a temperature of about 39° C. for a period of about 1 hr.

25. The method of claim 20, wherein said incubation is at a temperature of about 35° C. for a period of about 1 hr.

26. The method of claim 21, wherein said incubation is at a temperature of about 30° C. for about 1.5 hr.

* * * * *

EXHIBIT B

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

AUG 11 2009

Gail E. Poulos
USDA-ARS-OTT
5601 Sunnyside Avenue, Rm. 4-1183
Beltsville, Maryland 20705-5131

In Re: Patent Term Extension
Application for
U.S. Patent No. 5,135,759

Dear Ms. Poulos :

An interim extension under 35 U.S.C. § 156(d)(5) is enclosed extending the term of U.S. Patent No. 5,135,759 for a period of one year from the original expiration date, i.e., until August 4, 2010. A copy of the Federal Register notice, published on August 4, 2009 at 74 Fed. Reg. 38585, regarding the issuance of the interim extension under 35 U.S.C. § 156(d)(5) is also enclosed. While a courtesy copy of this letter is being sent to the Food and Drug Administration (FDA), you should directly correspond with the FDA regarding any required changes to the patent expiration dates which are pertinent to any filings before the FDA.

Inquiries regarding this communication should be directed to the undersigned by telephone at (571) 272-7755, or by e-mail at mary.till@uspto.gov.

Mary C. Till
Legal Advisor
Office of Patent Legal Administration
Office of the Deputy Commissioner
for Patent Examination Policy

cc: Office of Regulatory Policy
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 51, Rm. 6222
Silver Spring, MD 20993-0002

Attention: Beverly Friedman

RE: MicroSort® Sperm Separation Technology
FDA Docket No.:

UNITED STATES PATENT AND TRADEMARK OFFICE

In re United States of America as represented by the Secretary of Agriculture	:	
Request for Patent Term Extension	:	**ORDER GRANTING**
U.S. Patent No. 5,135,759	:	**INTERIM EXTENSION**

On June 8, 2009, patent owner, United States of America, as represented by the Secretary of Agriculture, timely filed an application under 35 U.S.C. § 156(d)(5) for an interim extension of the term of U.S. Patent No. 5,135,759. The patent claims a use of the medical device, the MicroSort® Sperm Separation Technology. The application indicates, and the Food and Drug Administration has confirmed, that a Premarket Approval application (P090004) for the MicroSort® Sperm Separation Technology has been filed by the licensee of the patent owner, Genetics & IVF Institute, and is currently undergoing regulatory review before the Food and Drug Administration for permission to market or use the product commercially.

Review of the application indicates that except for permission to market or use the product commercially, the subject patent would be eligible for an extension of the patent term under 35 U.S.C. § 156, and that the patent should be extended for one year as required by 35 U.S.C. § 156(d)(5)(B). Because it is apparent that the regulatory review period will continue beyond the original expiration date of the patent (August 4, 2009), interim extension of the patent term under 35 U.S.C. § 156(d)(5) is appropriate.

An interim extension under 35 U.S.C. § 156(d)(5) of the term of U.S. Patent No. 5,135,759 is granted for a period of one year from the expiration date of the patent, i.e., until August 4, 2010.

07/28/09
Date

John J. Doll
Acting Under Secretary of Commerce for Intellectual Property and
Acting Director of the United States Patent and Trademark Office